

# Topics in Primary Care Medicine

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## Fecal Occult Blood Screening and Evaluation for a Positive Test

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The American Cancer Society recommends annual fecal occult blood testing for all asymptomatic persons 50 years of age and older. This testing enhances the identification of disease, including an increased percentage of pathologically earlier cancer lesions—that is, Dukes' A and B stages. As yet, however, no data have shown improved colon cancer survival rates in screened persons. In writing this paper, we assume that early detection of colonic neoplasia by occult blood surveillance is worthwhile and that ongoing long-term clinical trials will eventually show the survival benefit of this practice.

Fecal occult blood screening of asymptomatic persons yields 2% to 6% positive tests. If annual screening recommendations were universally implemented, 3 million asymptomatic Americans would have a positive result and should receive further testing. Diagnostic evaluations for this group would cost between 500 million and 2.5 billion dollars. Thus, implementing colorectal cancer screening has a major impact on physician time and medical economics. Each asymptomatic patient with a test positive for fecal occult blood should be further evaluated in a thorough but cost-effective manner. Our discussion will focus on these issues and offer a practical approach to the evaluation of these asymptomatic patients.

### Methods of Fecal Occult Blood Testing

Seven commercial fecal occult blood tests based on guaiac-impregnated paper currently are available in the United States. Of these, only Hemoccult II has been objectively compared with other techniques—such as labeling erythrocytes with chromium 51 to detect blood loss—and has achieved widespread popularity. Hematest, a preparation based on or-

thotoluidine, is not recommended due to poor reliability, as it yields more false-positive and false-negative results. Several new methods for more specific or sensitive occult blood detection have been developed, and their usefulness is being explored. HemoQuant, a quantitative assay based on the conversion of heme to fluorescent porphyrins, is more sensitive for hemoglobin. Another test using immunochemical methods with anti-human hemoglobin also has a high true-positive rate free of cross-reaction with foodstuffs, animal hemoglobins and drugs. Both of these tests are technically complex, costly, time-consuming and not yet applicable for general use.

Effective cancer screening requires patient acceptance. The return of Hemoccult cards is frequently low, ranging from 26% in a mass screening program to 75% in a highly motivated patient group followed in a private practice setting. Developing screening methods in which the aesthetic aspects of stool sampling are improved may also increase compliance. An example of this is the recently released Coloscreen Self-Test, a chemically treated paper pad that is placed in the toilet bowl after a bowel movement and changes color to indicate a positive reaction. The patient is responsible for interpreting the test and reporting a positive result to the physician. There are only limited data suggesting concordance between Coloscreen testing and Hemoccult II, and no studies of Coloscreen Self-Test compliance have been published. Thus, Hemoccult II is currently the best standardized and most practical approach to widespread fecal occult blood screening.

Hemoccult II test paper is impregnated with gum guaiac. When a fecal specimen contains peroxidases or catalases (in-

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cluding hemoglobin), or both, a reaction occurs with hydrogen peroxide in the developer solution. This catalyzes the oxidation of guaiac to a quinone structure, which causes a blue color change. The Hemoccult II slide has a faint color change in the presence of 4 to 6 ml of hemoglobin per 100 grams of feces, which is twice the normal daily fecal blood loss in an adult. Guaiac testing is not specific for human hemoglobin, and a variety of foods and medications commonly affect the results (see Table 1). Other agents may also affect test interpretation under special circumstances. Cimetidine often produces a false-positive test of gastric aspirates but does not affect stool specimens. Povidone-iodine, used as a topical antiseptic or douche, may cause false-positive results due to oxidation by iodine, whereas the use of laxatives may increase the frequency of both false-positive and false-negative results. Of note, barium sulfate in the stool does not influence the reaction, nor does the use of a high-residue diet. Factors known to affect guaiac testing should be avoided starting 48 hours before the first stool collection and not resumed until all the stool specimens have been obtained. For screening purposes, specimens should not be taken if blood is actually seen in the stool, or urine, or if a patient is menstruating.

Using a protocol for stool collection and testing as listed in Table 2, the false-positive rate for Hemoccult II is acceptably low at 1% to 3%. The cost impact of small deviations from this type of protocol is significant. If, for example, an underlying 1% true-positive rate is assumed, with 1% false-positives, about 50% of positive Hemoccult tests will come from patients with neoplasia (cancer or polyps). With 3% false-positives, only 25% of positive Hemoccult tests will come from patients with neoplasia. Moving from a 1% false-positive rate to a 3% false-positive rate will substantially increase the cost of a screening program.

Because fecal occult blood testing relies on active bleeding to detect colonic lesions, a significant number of nonbleeding, minimally or intermittently bleeding lesions will be missed. To minimize the number of bleeding lesions missed, ascorbic acid must be avoided and slides must be returned promptly for immediate testing. A strong reaction will remain positive for at least ten days, whereas specimens with weakly positive reactions may yield negative or equivocal results after two or four days of storage. This is presumably due to desiccation of the fecal specimen with time. Attempts have been made to

increase the sensitivity of Hemoccult II to peroxidases by rehydration. Sensitivity improves, but specificity decreases, as rehydration produces more false-positive readings. Thus, it is not a generally recommended procedure.

Even when used optimally, Hemoccult II misses as many as 65% to 75% of colonic polyps and 10% to 30% of cancers. This has led the American Cancer Society to recommend flexible sigmoidoscopy as a complementary screening procedure. When carried out to 60 cm, sigmoidoscopy can detect greater than 60% of colon cancers and 60% of colonic polyps. This procedure can be done safely by community-based pri-

TABLE 1.—Factors Affecting the Results of Hemoccult II Testing

Drugs and Dietary Restrictions	Justification
Aspirin or nonsteroidal anti-inflammatory drugs . . . . .	Increased fecal blood loss in healthy persons documented by $^{51}\text{Cr}$ -labeled erythrocyte studies
Ferrous sulfate or ferrous gluconate . . . . .	Several small studies suggest a higher rate of false-positive tests for healthy persons using ferrous salts
Ascorbic acid . . . . .	Fecal excretion of ascorbic acid (> 55 mg/day) inhibits Hemoccult reaction
Rare red meat (beef, lamb) . . . . .	Excluding rare red meat (250 grams steak/day) from diet led to a significant fall from 6.1% to 1.6% in Hemoccult positivity
Fresh vegetables, fruits high in peroxidase . . . . .	Peroxidase in 5 to 10 grams of uncooked radish, horseradish, cantaloupe or cauliflower has an activity equivalent to 1.0 ml of blood

TABLE 2.—Protocol for Stool Sample Testing

Two days before the first stool collection and continuing throughout the collection period, avoid ingestion of aspirin, nonsteroidal anti-inflammatory drugs, vitamin C, iron, laxatives, rare red meat and fruits and vegetables high in peroxidases (Table 1).\*

Beginning on the third day of the diet, take two specimens from three consecutive stools.

Promptly return the three completed Hemoccult cards (six samples). Test samples promptly.

Evaluate all positive results.

\*Other foods with moderately high peroxidase content (cucumbers, carrots and grapefruit) should be avoided in excessive amounts.

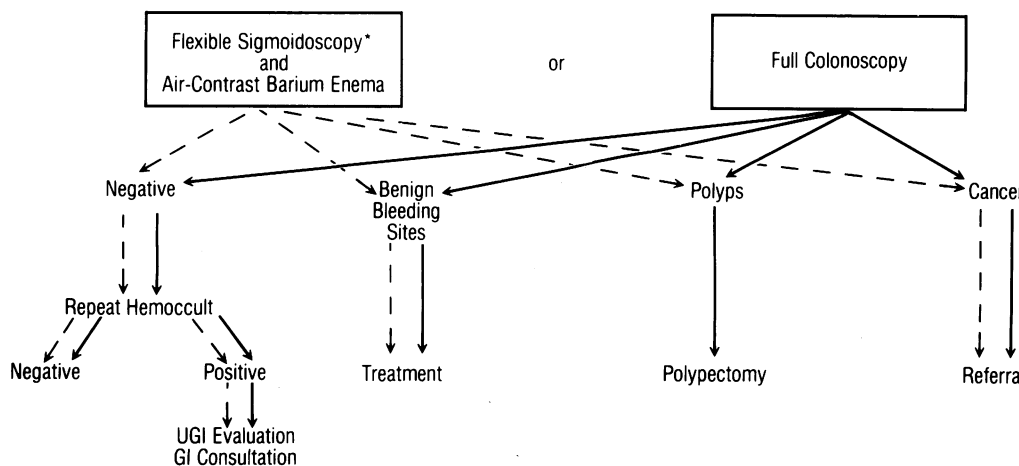


Figure 1.—Evaluating an asymptomatic patient with a Hemoccult-positive test. \*If polyps are found by flexible sigmoidoscopy, then an air-contrast barium enema should be replaced by full colonoscopy. GI = gastrointestinal, UGI = upper gastrointestinal [tract]

mary care physicians in asymptomatic Hemoccult-negative patients with a diagnostic yield of 10% neoplasia (9% polyps, 1% cancer).

### Evaluation for Tests Positive for Fecal Occult Blood

Once a screening Hemoccult test is positive in an asymptomatic patient, it cannot be ignored, and further evaluation is warranted. Subsequent negative Hemoccult tests do not adequately rule out neoplasia, as bleeding can be intermittent. The challenge lies in choosing the best procedural algorithm that will detect the highest percentage of colonic polyps and cancer with the least risk and the lowest cost. Controlling costs means minimizing the direct costs of the procedure and physician fees and the indirect costs of complications of the procedure, patient anxiety, time lost from work and evaluation for false-positive tests. Physicians must also consider the relative strengths and availability of resources in their communities.

Two approaches meet these needs: (1) flexible sigmoidoscopy to 60 cm, plus air-contrast barium enema, or (2) full colonoscopy (Figure 1). If colonoscopy is done initially, it provides an adequate identification of colonic pathology. It generally is the most sensitive procedure for detecting polyps. If colonic preparation is poor, however, or if the colonoscope is not able to reach the right side of the colon, as many as 10% of polyps may be missed. The major risk of colonoscopy is perforation, which occurs in about 3 per 1,000 patients screened. This rate is about tenfold higher than the perforation rate of a barium enema. But because colonoscopy has the major advantage of using one procedure to endoscopically examine and take a biopsy of the rectosigmoid and more proximal colon, it is being used more frequently for the initial evaluation of patients with a positive Hemoccult test. Because colonoscopy is usually done by gastroenterologists or surgeons, a limitation is accessibility to the procedure. In some communities, flexible sigmoidoscopy and air-contrast barium enema (ACBE) are more practically done than colonoscopy.

Flexible sigmoidoscopy can be done by primary care physicians as well as specialists. It is preferable to rigid sigmoidoscopy because it leads to the detection of at least twice as many polypoid lesions. Patients with flexible sigmoidoscopic examinations in which the results are normal or who have benign bleeding sites identified should then have a good-quality ACBE. Patients with rectosigmoid polyps

should bypass the ACBE and have a full colonoscopy to detect and remove any additional polyps. If cancer is found on flexible sigmoidoscopy, the patient should have an ACBE or full colonoscopy to further define the tumor involvement and rule out synchronous colon cancer, which occurs in 4% to 6% of these patients.

The air-contrast barium enema, if done with adequate colonic preparation and radiologic technique, is as sensitive (92% to 98%) as colonoscopy in detecting carcinoma of the colon, excluding anal or rectal lesions and in situ cases. It has the advantage of providing a permanent record of each examination. If the colonic cleansing is poor, however, or if a single-column barium enema is done, as many as 30% of Dukes' C and D tumors and 60% of Dukes' A and B tumors may be missed by barium enema. In addition, ACBE is less sensitive for detecting polyps. Several studies comparing ACBE and colonoscopy have shown that ACBE may miss 25% to 50% of polyps less than 1 cm and 10% to 25% of polyps greater than 1 cm. About 85% of the radiologically undetected polyps larger than 5 mm, however, are located in the sigmoid colon and flexible sigmoidoscopy complements ACBE by detecting polyps in this location.

Assuming strict adherence to the protocol of stool sampling as in Table 2, about half of asymptomatic patients with a positive Hemoccult test will have significant colonic neoplasms, with polyps larger than 5 mm outnumbering cancers (38% versus 12%). Of the total number, 30% will have benign sites of possible colorectal bleeding identified—such as diverticulosis, polyps smaller than 5 mm, internal hemorrhoids—and 20% will have normal lower gastrointestinal tract studies. This latter group of patients should undergo repeat Hemoccult testing followed by upper gastrointestinal tract evaluation or consultation with a gastroenterologist if tests are persistently positive. Hemoccult testing is relatively specific for lower gastrointestinal tract bleeding. About 80% of asymptomatic patients with a positive Hemoccult test will have a colonic bleeding site identified by a thorough evaluation.

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